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REVIEW ON DRUG APPROVAL PROCESS IN KENYA, TANZANIA, INDIA, CHINA

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ABSTRACT

This study contains comparison of drug approval requirements between various regulated and non-regulated markets that could result in a clear understanding of the market positions of different countries and most importantly revise regulations for a healthier tomorrow. The overall objective of a stringent drug approval system is to ensure that medicinal products of acceptable quality and efficacy are manufactured. The pharmaceutical industry is one of the highly regulated industries, to protect the health and well-being of the masses This topic aims to explain and compare the different processes and regulations for approval of drugs in regulated and non-regulated market. As per law, all new drugs must first be shown to be safe and effective before they can be approved for marketing. Many of the generics produced are now constitute in all parts of the world. A regulated market is the regulations of services that is regulated by a government authorization body. Drug authorization standards in regulated countries are considered by many to be the most exacting in the world. Discovering a new drug, and crafting it through various review process, can take many years. To a large degree, these costs are mostly associated with the clinical testing. Coming to authorization of drugs in typical non-regulated markets, they are becoming an important player in drug manufacture, in particular, the production of generics.

KEYWORDS: To a large degree, these costs are mostly associated with the clinical testing.

INTRODUCTION

Regulatory Affairs departments are growing within companies & is constantly evolving and growing and is the one, which is least, impacted during the Acquisition and Merger, and

during recession. Global harmonization in standards has led to consistent approach in regulatory submissions and hence its review.

A regulatory process in which an organization/ innovator/ sponsor/ person gets approval to establish a drug in the market is called drug approval process. Comprises at various stages application consist of clinical trials, application to marketing authorization of drug and post marketing studies every country has its own regulatory authority, having an overall objective of a stringent drug approval system is to ensure that medicinal products of acceptable quality and efficacy are manufactured.

Global Market is divided into

1. Regulated Market: US, EU (UK, Germany, France, Ireland, Sweden etc.), Japan, Canada, Australia, New Zealand, South Africa

2. Semi regulated Market: (ROW Countries)

(a) Asia (Sri Lanka, India, Bangladesh, ASEAN: 10 Countries group - Philippines, Vietnam Singapore, Malaysia, Thailand, Indonesia, Laos, Cambodia, Brunei Darussalam, Myanmar.

b) African countries (Algeria, Zambia, Ethiopia, Ghana, Kenya, Malawi, Mozambique, Namibia, Nigeria, Sierra Leone, Tanzania, Zimbabwe etc.).

(c) Middle East countries (Gulf Co-operation Council countries i.e. Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, UAE).

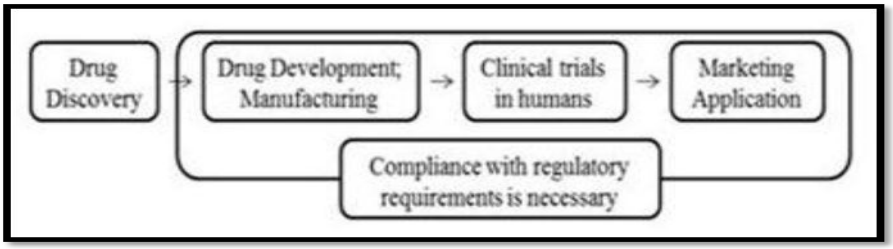
(d) Latin America (Mexico, Brazil, Panama, Peru, Guatemala, Argentina, Chile, Dominican Republic).

(e) CIS (common wealth of independent states): Russia, Ukraine, OFSUs (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kirghizstan.

Difference from Regulated Market

Degrees of implementation are different. Intensity of audits/ inspections is different and similarly penalties for GMP violations are different. Regulated market guidelines are very clear and are to be adhered to 100%.

METHODS



1. General Regulatory Filling Procedure

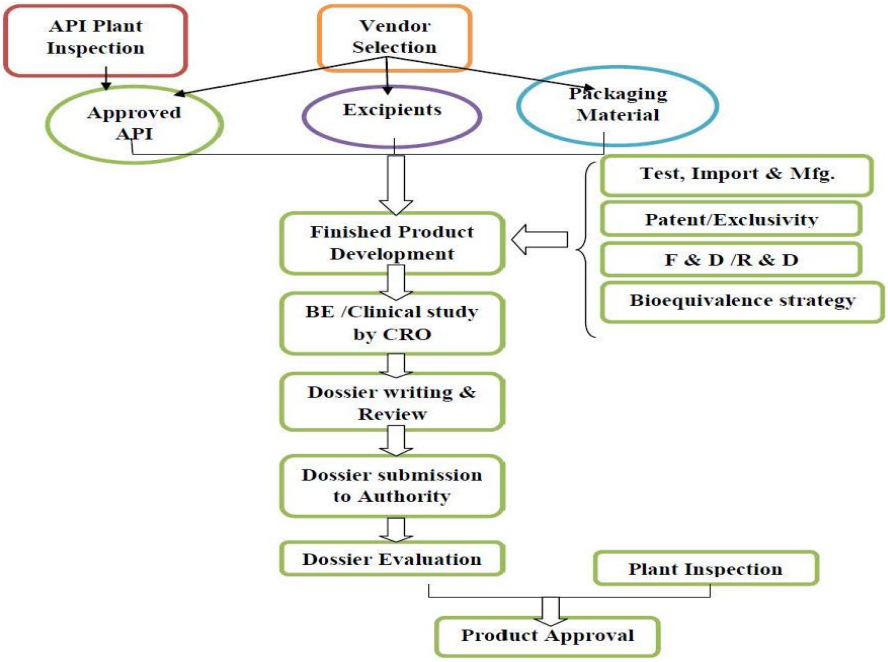


Figure No.1: General Regulatory approval process.

Filling Strategy of Regulatory Requirements

Table 1: Filing Strategy of Regulatory Requirements of African Countries.

Filing Strategy of Regulatory Requirements of African Countries				
	Requirements	**Kenya**	**Tanzania**	**Uganda**
	MOH	PPB: Pharmacy and poisons board	TFDA: Tanzania and food and drug administration	NDA: National drug authority
Plant	Dossier Format	CTD	CTD-Country specific	CTD
	cGMP Inspection	Required	Required	Required
	cGMP Inspection Fee	Required	Required	Required
	Validity period	3	5	3
	Admin documents	Mf.lic, GMP(Notarized), CPP(Notarized)	Mf.lic, GMP, FSC, CPP	Mf.lic(Notarized), FSC, CPP(Notarized)
	Artworks	English/ Anglo-French	English/ Anglo-French	English/ Anglo-French
	Sample requirements	8packs	6packs	5packs
Product	Stability data	30/65(6Months)	30/65(6Months)	30/65(6Months)
	Registration fee	USD 1000.00	USD 750.00	USD 1250.00
	Registration lead time	12-18 Months	6-9 M (Fast track), 9-18M (Normal)	12-18 Months
	Registration validity	1(Every year retention fee should be submitted)	5	1(Every year retention fee should be submitted)
	Retention fee	USD 300.00	USD 100.00	USD 300.00

KENYA

1. Drug Regulatory Agency: Pharmacy and Poisons Board
2. Language: English
3. Format Followed: CTD
4. Type of Registration

a. New Application for Registration

A new application for registration shall include submission of

1. Two dully filled application forms (Original and duplicate) and an electronic copy (a summary of the dossier contents) in MS Word on a CD-ROM of modules 1 and 2 only including their supporting documents.
2. Three (3) samples of the smallest commercial pack(s) from one batch with batch certificates of analysis.
3. An original Certificate of Pharmaceutical Product (WHO Format) on official papers of the issuing competent drug regulatory authority.
4. A site master file in case the product is manufactured at a plant(s) not inspected and approved by PPB.
5. Non-refundable application fee for registration of medicines in Kenya and GMP inspection fees for facilities not yet inspected by PPB.

b. Applications for Renewal of Registration: Applications for renewal of registration shall be made at least 3 months before the expiry of existing registration by submitting the following:

- ✓ Dully filled in application form for renewal of registration.
- ✓ Batch Manufacturing Record (BMR) of a real batch manufactured within at most six months before the submission of the application.
- ✓ Submit Periodic Safety Update Reports (PSUR).
- ✓ Proof of interchange ability for generics as explained in Module 5.
- ✓ Any other requirements that the Board may determine.
- ✓ Three (3) samples of the smallest commercial pack(s) from the same batch along with batch certificates of analysis.
- ✓ A site master file in case the product is manufactured at a plant(s) not inspected and approved by PPB.
- ✓ Nonrefundable application fee for registration of medicines in Kenya and GMP inspection fees for facilities not inspected and approved by PPB, GMP department.

c. Application for Variation of a registered medicinal product

All applications for variation to a registered product shall be made according to requirements stipulated in the PPB Application Guideline for Variation of Registered Medicinal Products also available the PPB offices.

d. Drug Approval process in Kenya

The drug regulatory agency in Kenya is the Pharmacy and Poisons Board, which was established under the Pharmacy and Poisons Act, Chapter 244 of the Laws of Kenya. It takes approximately 90 working days for fast-tracked drug registration. Fast-tracked applications include locally-manufactured and priority medicines only. The drug application is considered withdrawn if queries are not adequately responded to within 6 months of the request. If a drug is declined, the applicant may appeal that decision within 2 months from the date of notification. Drug Registration is valid for 5 years unless otherwise suspended or revoked.

Table 2: Cost of Drug Application in Kenya.

Imported into Kenya	$1000
Fully manufactured in Kenya	$500
Renewal of application(local)	$300
Renewal of application (imports)	$500

e. Stability Conditions: Zone II, Iva

General Requirements

Table 3: Storage requirement for Stability.

Sr. No.	Study	Storage Conditions	Minimum time Period Covered (months)
1	Long term	30±2◦C / 65±5% RH or 30±2◦C / 75±5% RH	12
3	Accelerated	40±2◦C / NMT 75±5% RH	6

TANZANIA

1. Drug Regulatory Agency: Tanzania and Food and Drug Administration

2. Language: English

3. Format Followed: CTD

4. General Information on format used: The Tanzania Food and Drugs Authority (TFDA) was established under the Tanzania Food, Drugs and Cosmetics Act, Cap 219 with the mission of protecting and promoting public health by ensuring quality, safety and effectiveness of food, drugs, cosmetics and medical devices.

The "Guidelines on Submission of Documentation for Registration of Human Pharmaceutical Products' First Edition, January 2015" is the TFDA publication, which sets out procedures and requirements for the implementation of Pharmaceutical Products Registration through Common Technical Document (CTD). The CTD has five Modules. Another requirement as per prescribed in introduction of regulatory requirements

5. Stability Conditions: Zone II, IVb General Requirements.

General Requirements.

Table 4: Stability Conditions: Zone II, IVb General Requirements.

Sr. No.	Study	Storage Conditions	Minimum time Period Covered (months)
1	Long term	30±2◦C / 65±5% RH or 30±2◦C / 75±5% RH	12
2	Long term (product intended to storage in a refrigerator)	5 ◦C ± 3◦C	12
3	Accelerated	40±2◦C / NMT 75±5% RH	6
4	Accelerated((product intended to storage in arefrigerator)	NMT 65±5% RH or 30±2◦C / NMT 75±5% RH	6

6. Fee Requirements

Person shall pay a fee prescribed in the Schedules in respect of the products and services regulated under the Tanzania Food, Drugs and Cosmetics Act. Fees and charges paid under the Regulations shall be paid in Tanzanian shillings or US$ equal to the amount of Tanzania shillings or any convertible shilling equal the amount payable in Tanzania Shillings. Fees and charges paid under the Regulations shall be collected and appropriated by the Authority. The Authority may appoint an agent or any local Authority within the area the fees paid, and charges operates to be a collecting agent. Fees and charges payable under the Regulations shall not be refundable or transferable.

Failure to pay in time the fees and charges in force shall, in addition to the due charge, pay a penalty of 25% of the total amount payable.

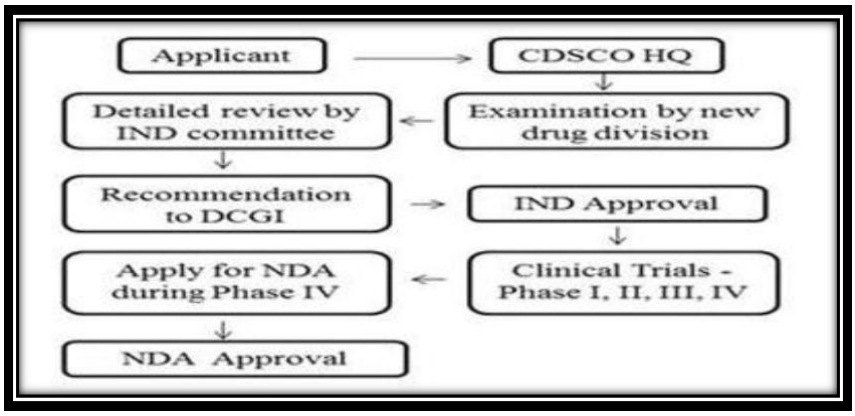
Table 7: TFDA Fees and Charges Structure for Registration/ Retention/ Notification/ Variation.

Human and Veterinary medicines (Domestic)		
Sr. No.	**Service**	**Fee**
1.	Registration	USD 500
2.	Variation –Major	USD 100
3.	Variation –Minor	USD 50
4.	Retention	USD 150
5.	Duplicate Certificate	USD 50
	Human, Veterinary Medicines and Biologicals (Imported)	
6.	Registration	USD 2000
7.	Registration – biological	USD 3500
8.	Retention	USD 300
9.	Variation – major	USD 1000
10.	Variation – minor	USD 300
11.	Duplicate certificate	USD 100
12.	Fast track registration-Pharmaceuticals	Double the respective fee

Drug Approval in India

Increasingly, India is becoming an important player in drug manufacture, in particular, the production of generics. Many of India's generics are now found in all parts of the world, challenging the dominance once held by the large pharmaceutical companies in Western countries. Under India's Drugs & Cosmetics act, Central Drugs Standard Control Organization (CDSCO) controlled by DCGI, is the Central Drug Regulating Agency responsible for approving new drugs, clinical trials, & maintenance of standard of drugs, jurisdiction of importation of foreign drugs, approval of manufacturing licenses & coordination of activities of the State Drug Control Organizations. The central government is also responsible for the testing of drugs by the central drug labs, whereas the state authorities are responsible for the regulation of the manufacture, sale & distribution of drugs. Schedule Y of D&C rules sets up the requirements for clinical trials & that of schedule M for GMP compliance system.

The Approval process in India



- The drug approval process varies from one country to another. Other issues where the difference appears are, time taken for the approval of a CTA application, time taken in evaluation of marketing authorization application, registration fee, registration process & marketing exclusivity.
- Globally clinical trials are classified into 2 categories
- Category A: It includes clinical trials whose protocols have been approved by USA, UK, Switzerland, Australia, Germany, Canada, South Africa, Japan & Europe for which DCGI will reach to a decision whether to approve the trial within 2 - 4 weeks
- Category B: It includes clinical trials whose protocols have been approved in other countries which are not listed in Category A for which the DCGI turnaround time for these applications will be 8 - 12 weeks.
- Some counties have two review processes as normal review process & accelerated review process as in USA, China etc. & some countries have only a single review process as in India.

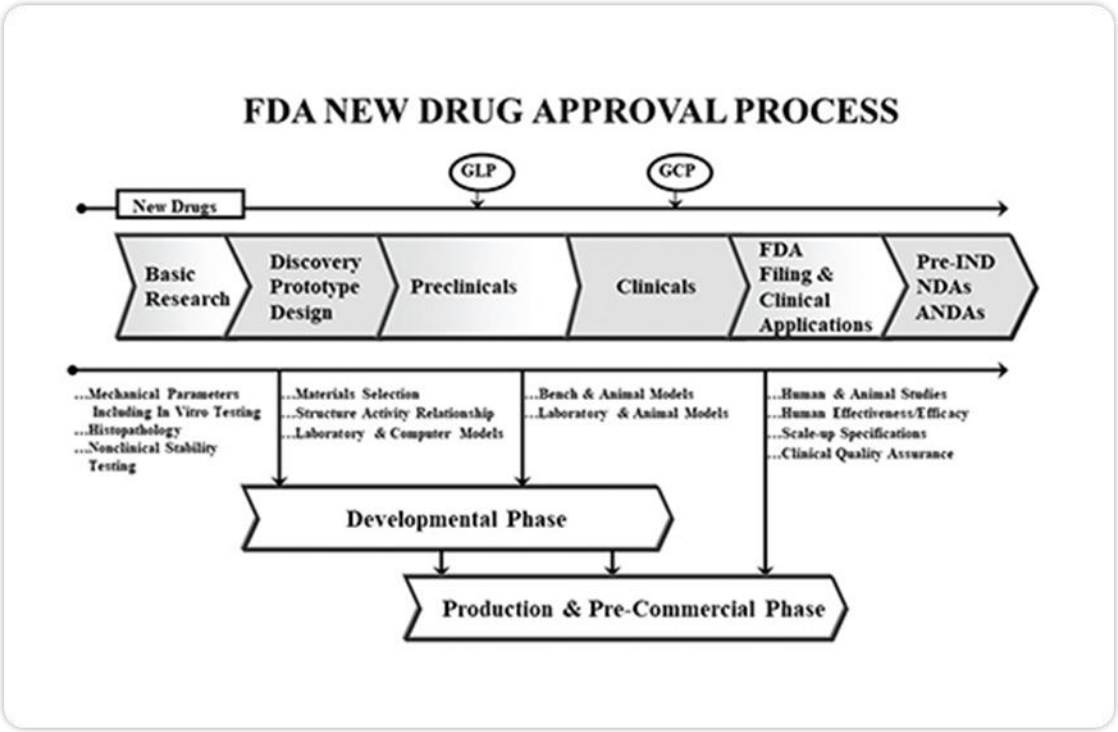
Drug Approval in China

China's Pharmaceutical market is growing at a very fast pace. The current data shows that the total market is around US$20 billion & is the 9th largest pharmaceutical country in the world. China's market is expected to be the world's largest market by 2020.

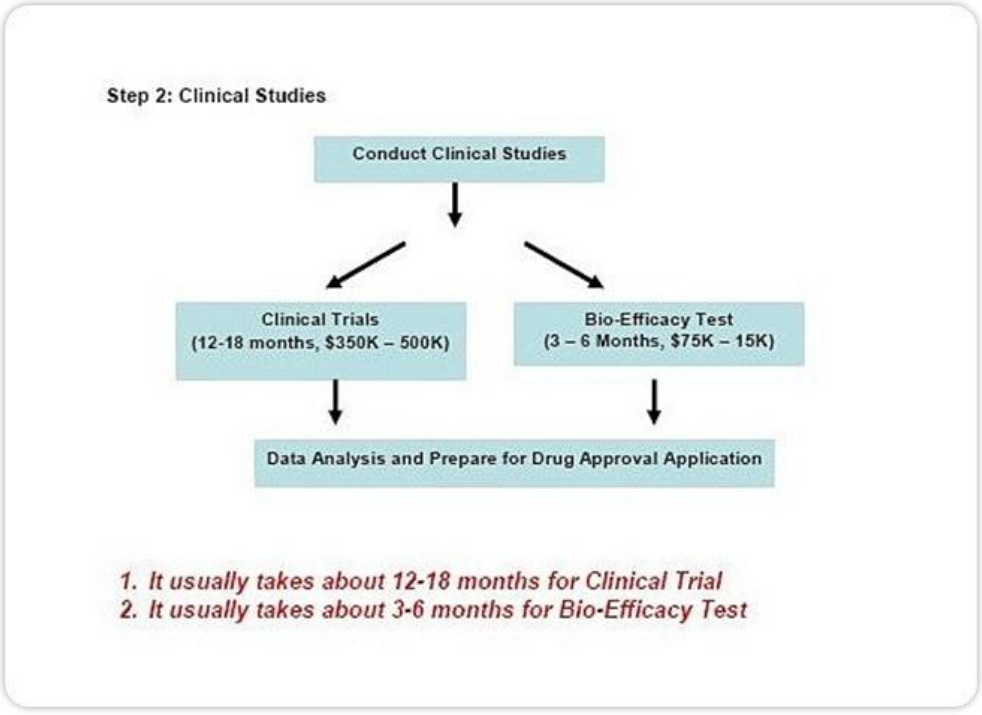
The regulation of drugs in china is under the jurisdiction of State Food & Drug Administration (SFDA) which is under control of the state council. The SFDA manages the regulation for "Western" drugs and Traditional Chinese.

Medicine (TCM) under the Division of Pharmaceuticals, Division of Biological Products, and Division of TCM of the DDR.

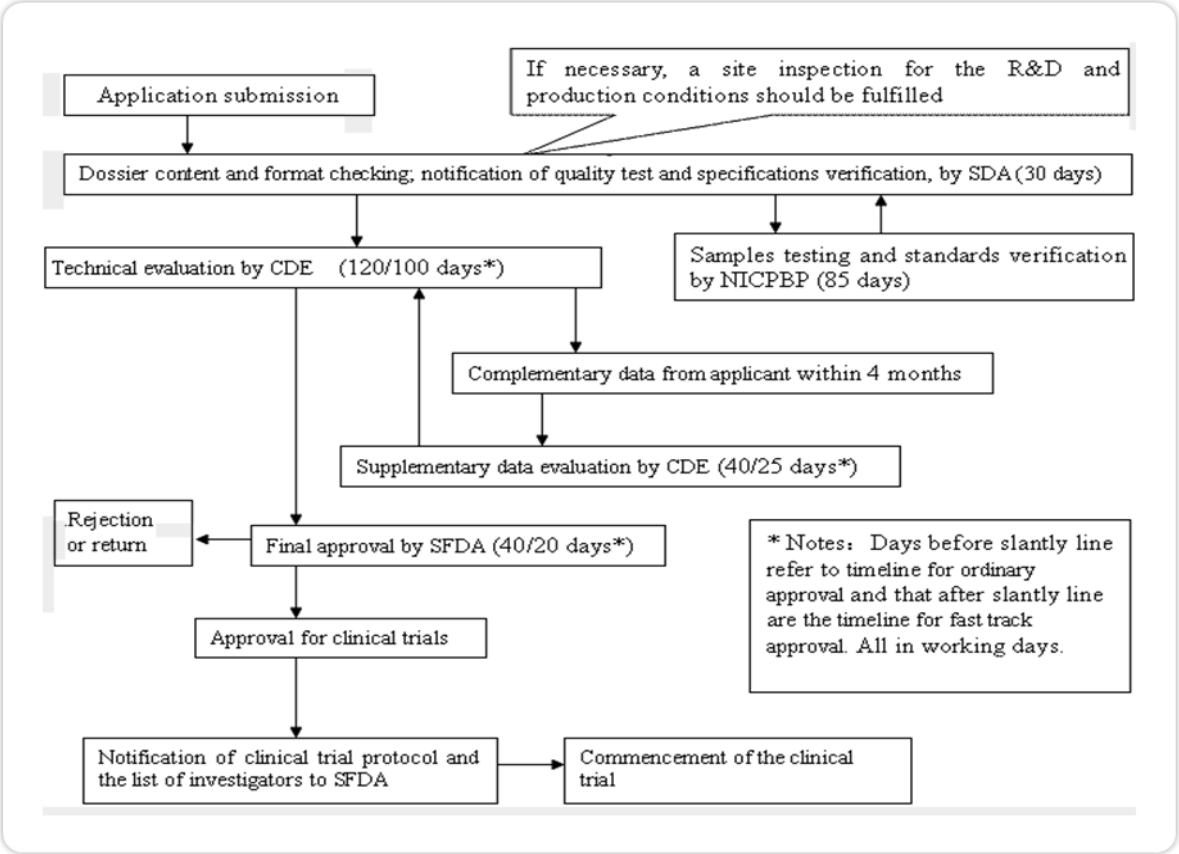
China offers a large pool of treatment naive patients for clinical trials. Clinical trials are one - third the cost of that in the United States and recruitments are expected to be rapid.



Step 1 - Application for approval of New Drug.



Step 2 - Clinical Trials.



Step 3 - Application and approval procedure for drugs (1)-China FDA, SFDA, CFDA, MOH, MOA, AQSIQ, CNCA, CIQ registration.

CONCLUSION

- A dossier containing detailed information about the drug and results of the studies carried out in its development process has to be submitted to the regulating bodies for getting market authorization. CTD is critical for dossier submissions.
- Any export market demands good quality dossier which can be generated through systematic Formulation Development.
- The proper planning and execution of Formulation development will help in quality dossier & in answering queries from Regulatory authorities.
- Since the world is divided in the drug approval procedures with technical data as described above, it is important especially for the generic manufacturers, to carefully judge the market need, Development Cost, target regions, & regulatory requirements before the development of drugs. Hence it is critical to plan and co-ordinate all the activities for successful launch of product in the market on time.
- As the regulatory requirements of various countries vary from each other, it is challenging for pharmaceutical companies to develop a drug formation, which can be simultaneously

submitted in numerous countries for approval at the same time. Therefore, continuous process of harmonization is taking place all over the world, still we can see a huge challenge, which is yet to be overcome by the pharmaceutical industry in case of generic drug development and filing as it involves strategic planning.

- Hence, one should carefully understand and define the clear regulatory strategy by looking at the target regions, different patent terms and its extension, various application possibilities, data requirements, potential timeline for marketing launch in different regions. This eliminates unnecessary studies, minimizes the delay in drug approvals and subsequent launch, and reduces overall cost of development

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